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Implementation of Diagnostics in Resource-Limited Settings

Amy Piatek

Global Health Bureau, Office of Health, Infectious
Diseases & Nutrition

U.S. Agency for International Development

Washington DC

apiatek@usaid.gov

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- Need for better TB and HIV diagnostics
- Implementation of TB Diagnostics:
 - Global uptake of Xpert MTB/RIF
 - Strategic approaches for Xpert MTB/RIF implementation and lessons learned
- TB and HIV integrated systems strengthening



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Need for Better TB and HIV Diagnostics



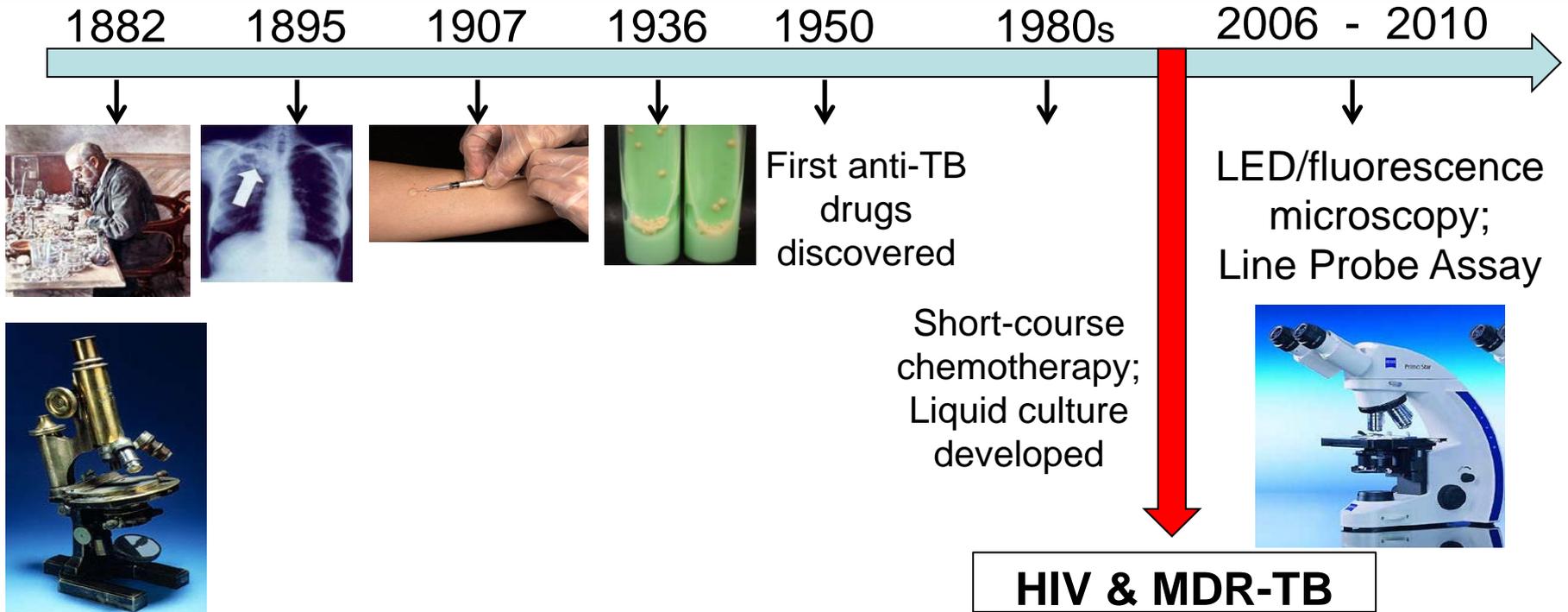
The Global Burden of TB

| | Estimated number of cases, 2012 | Number of cases diagnosed, 2012 |
|------------------------|----------------------------------|---------------------------------|
| All forms of TB | 8.6 million (8.3–9.0 million) | 5.7 million (66%) |
| HIV-associated TB | 1.1 million (1.0–1.2 million) | ~600,000 (55%) |
| Multidrug-resistant TB | 450,000 (300,000-600,000) | 94,000 (21%) |

Source: WHO Global Tuberculosis Control Report 2013



Evolution in TB Diagnostics



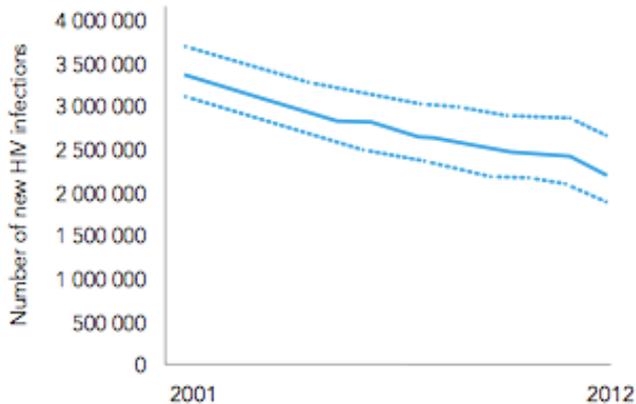
- Sputum smear microscopy is most commonly used in most resource-limited settings to detect TB.
 - Limitations: NTM, low sensitivity esp PLHIV, DR
- Sophisticated laboratories have been required to detect drug resistance
 - Limitations: biosafety, trained staff, time



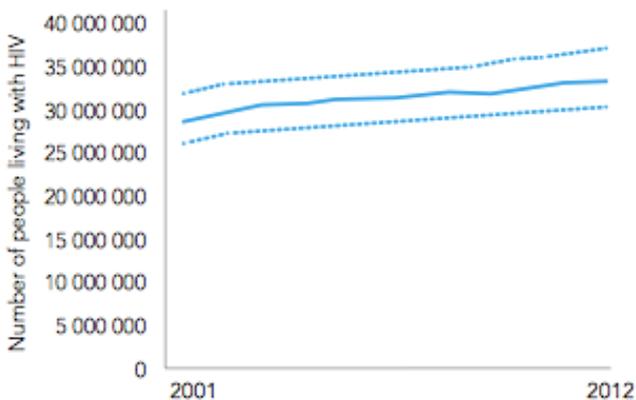
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New HIV infections and Number PLHIV, 2001-2012

NEW HIV INFECTIONS, GLOBAL, 2001-2012



PEOPLE LIVING WITH HIV, GLOBAL, 2001-2012



- Tests are required for **initial diagnosis**, **staging** and ongoing **monitoring** of HIV
- Those with most persistent challenges to improved access and efficiency are **CD4**, **viral load** and **EID**
- For these 3, most testing options available are:
 - Lab-based platforms using sophisticated instrumentation, dedicated lab space and trained lab staff
 - Mostly expensive
 - Require sample transport networks

Scale up of HIV services Has Required Scale Up of Lab Systems

| Type | Point-of-Care (POC) Available? | Availability |
|---|--|---|
| HIV diagnosis (antibody testing) | Yes | Widely available |
| HIV diagnosis (molecular) Early infant diagnosis (DNA, RNA, TNA, ultrasensitive p24) | In development | Use of dried-blood spots (DBS) has increased availability |
| Patient monitoring | CD4—yes, PIMA VL—in development | Use of DBS specimens |
| Toxicity monitoring (Hb, creatinine, chemistry, LFTs) | Needed | Variable |
| Diagnosis of opportunistic infections | Xpert, syphilis and malaria, rapid tests | Variable |
| HIV drug resistance surveillance | No | Periodic surveys recommended |
| Support to lab systems | n/a | Quality assurance, support for national strategic lab plans and a tiered laboratory network, human resource capacity building |



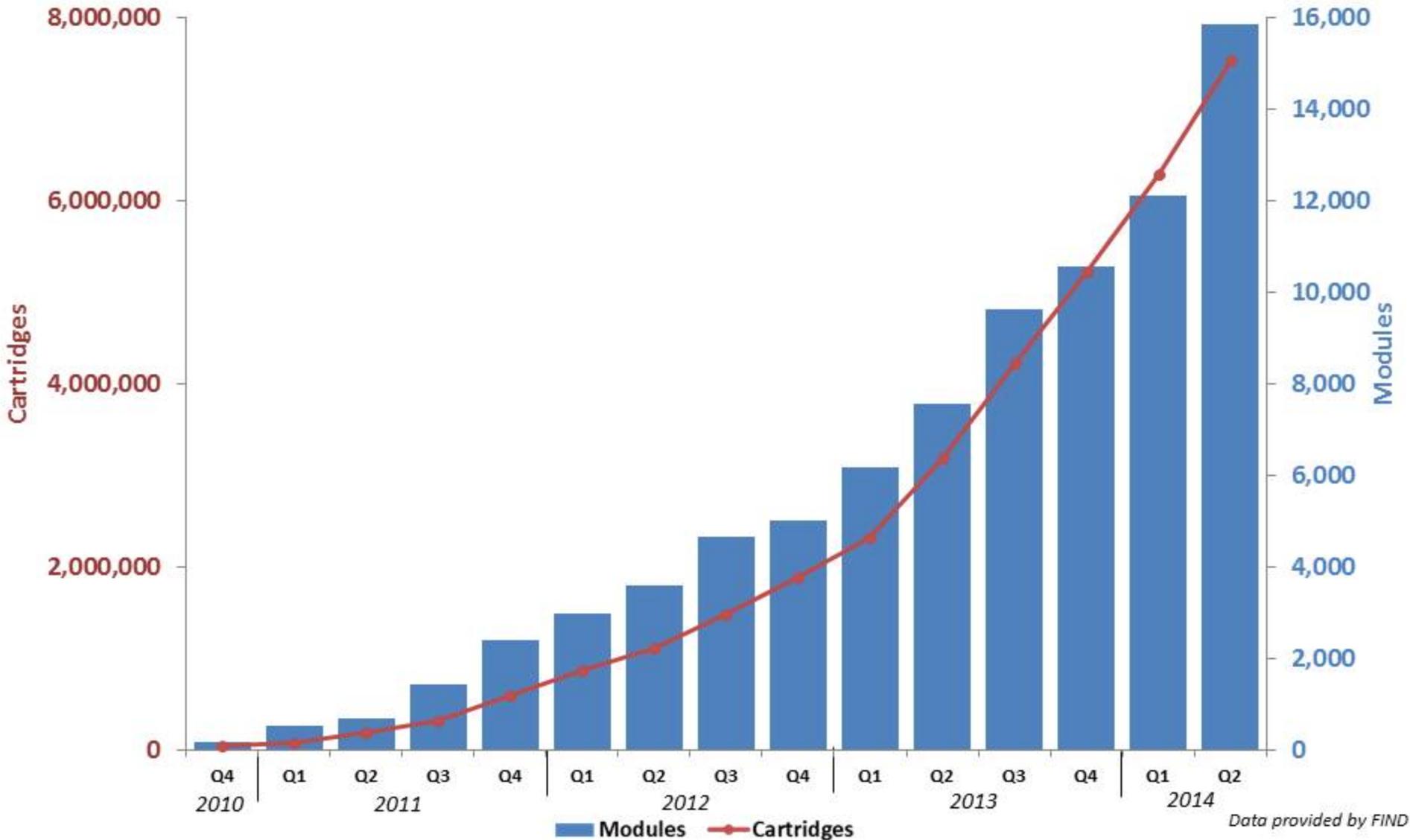
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Implementation of TB Diagnostics:

Example -- Global Uptake of Xpert MTB/RIF

Acknowledgement: Wayne Van Gemert, WHO Geneva

Cumulative number of GeneXpert instrument modules and Xpert MTB/RIF cartridges procured under concessional pricing



As of 30 June 2014, a total of 3,269 GeneXpert instruments (comprising 15,846 modules) and 7,531,360 Xpert MTB/RIF cartridges had been procured in the public sector in 108 of the 145 countries eligible for concessional pricing.

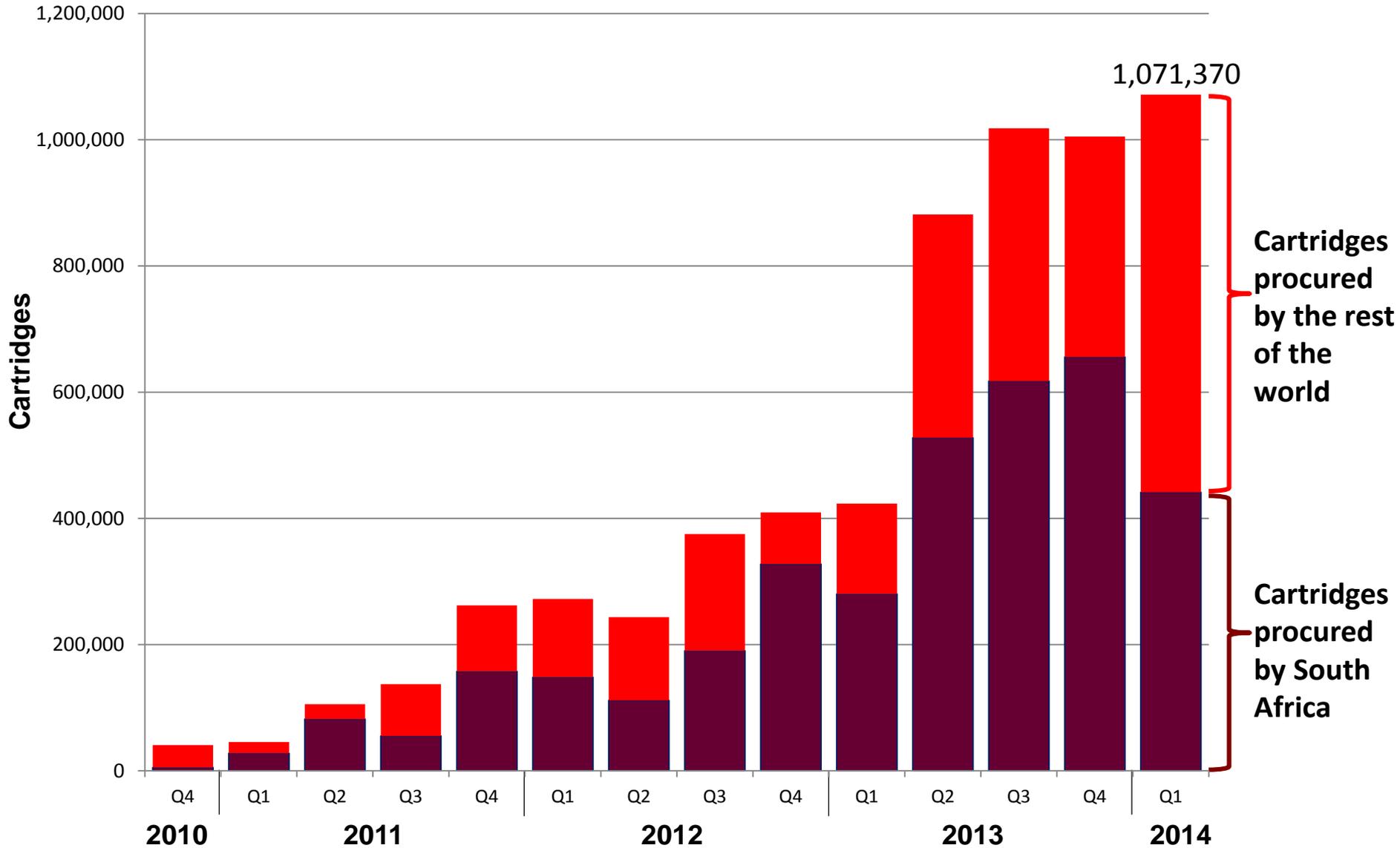


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Large Scale Xpert MTB/RIF Initiatives

- **TB REACH**: a Stop TB Partnership initiative funded by CIDA that focuses on TB case finding activities
 - Has procured over 150 Xpert machines and more than 250,000 Xpert MTB/RIF cartridges
 - **TBXpert**: a 3-year UNITAID-funded collaboration implemented by WHO and STB providing ~\$26m for roll-out of Xpert MTB/RIF in 21 countries
 - Private sector initiatives in Bangladesh, Indonesia and Pakistan (**IRD** social business model) and India (**IPAQT** project coordinated by CHAI)
 - USAID/CDC **PEPFAR** project of \$11m to support TB/HIV case finding using Xpert MTB/RIF in 14 high burden countries
 - Country scale-up
 - **South Africa**: 4,117 modules (as of March 2014, WHO/FIND)
 - Brazil: 716 modules
 - China: 716 modules
- } between 2013-2014*

Quarterly number of Xpert MTB/RIF cartridges procured under concessional pricing



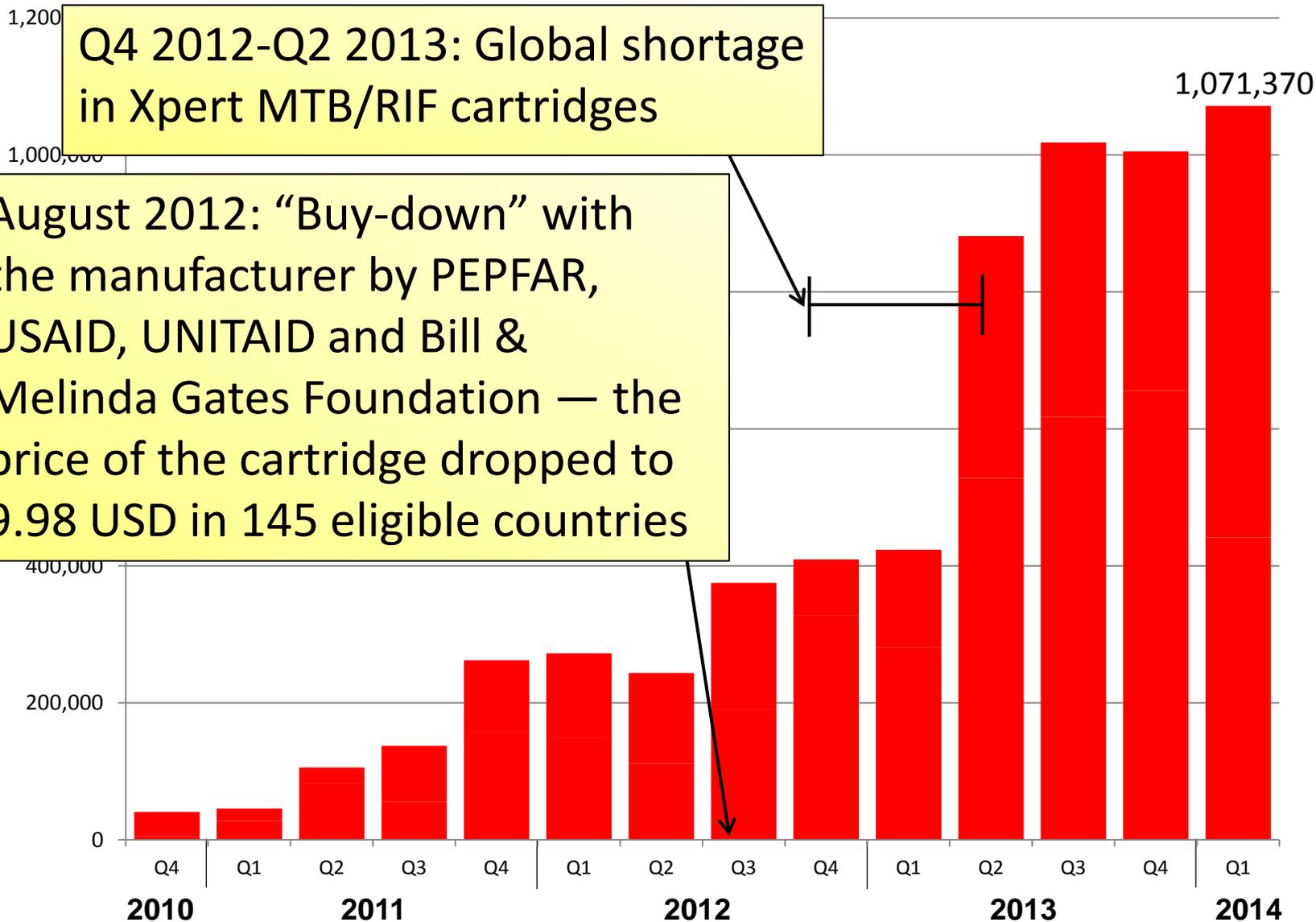


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Factors Supporting Scale-up

- WHO endorsement in Dec 2010
- Policies and recommendations (strong and conditional) for use of Xpert MTB/RIF according to type and risk group –
 - Evaluated through GRADE process and expert group consensus
- Early and documented experience of South Africa, implementing partners (MSF, TB CARE I, etc.)
- Cartridge price reduction through donor consortium (from \$16.86 to \$9.98)

Quarterly number of Xpert MTB/RIF cartridges procured under concessional pricing





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Strategic Approaches for Xpert MTB/RIF Implementation and Lessons Learned

Acknowledgement: TB CARE I



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Xpert MTB/RIF Technical Framework for Implementation

Joint USG approach – USAID/CDC/PEPFAR

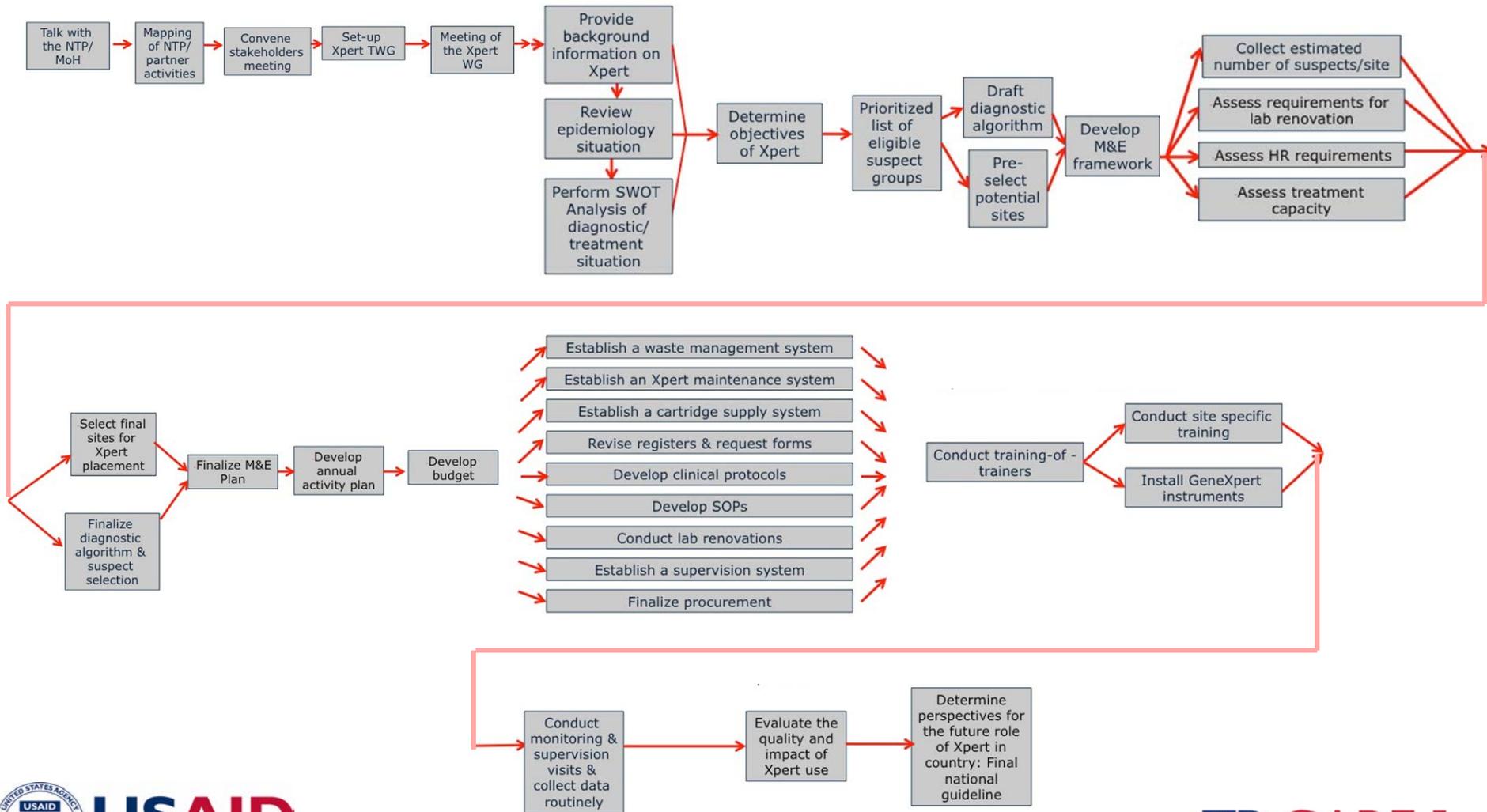
Comprehensive package of support and technical assistance

- Led by Ministry of Health
- Assessment of priorities, gaps, and stakeholders
- Formation of national GeneXpert advisory team
- Development of an implementation and quality assurance plan
- Preparation of testing sites and procurement of machines/tests
- Training of laboratory and clinical staff
- Monitoring and evaluation; operations research

Emphasis on systems strengthening to address entire diagnostic cascade (and links to treatment)

- Specimen transport networks
- Reporting of results – cascade to clinicians, patients, managers
- Supply management

Critical pathway to Xpert implementation





Lessons Learned: Xpert MTB/RIF Implementation

| Planning phase | Introduction phase | Uptake phase |
|--|--|--|
| Little global awareness of demonstration studies | Technical assistance needs extensive: operational and programmatic requirements | Diagnosis is outpacing capacity to treat MDR-TB: ensure links to quality treatment |
| Endorsement not timed to thought-out implementation | MoH must own and drive Xpert implementation: integrated strategy, no “one size fits all” | Where appropriate, shift diagnostic algorithm from focus on DR-TB to HIV-associated TB or other groups |
| Initially thought that very little, if any, technical assistance would be needed | Xpert assay cannot operate optimally in a struggling TB program | Continuously gauge machine utilization, couple with a strong logistics management system (expiring cartridges) |
| | M&E is essential to show impact and inform policy | Sustainability issues – how will countries pay for cartridges and scale-up? |
| | | Focus on <u>overall</u> diagnostic platforms to ensure uptake of followers |

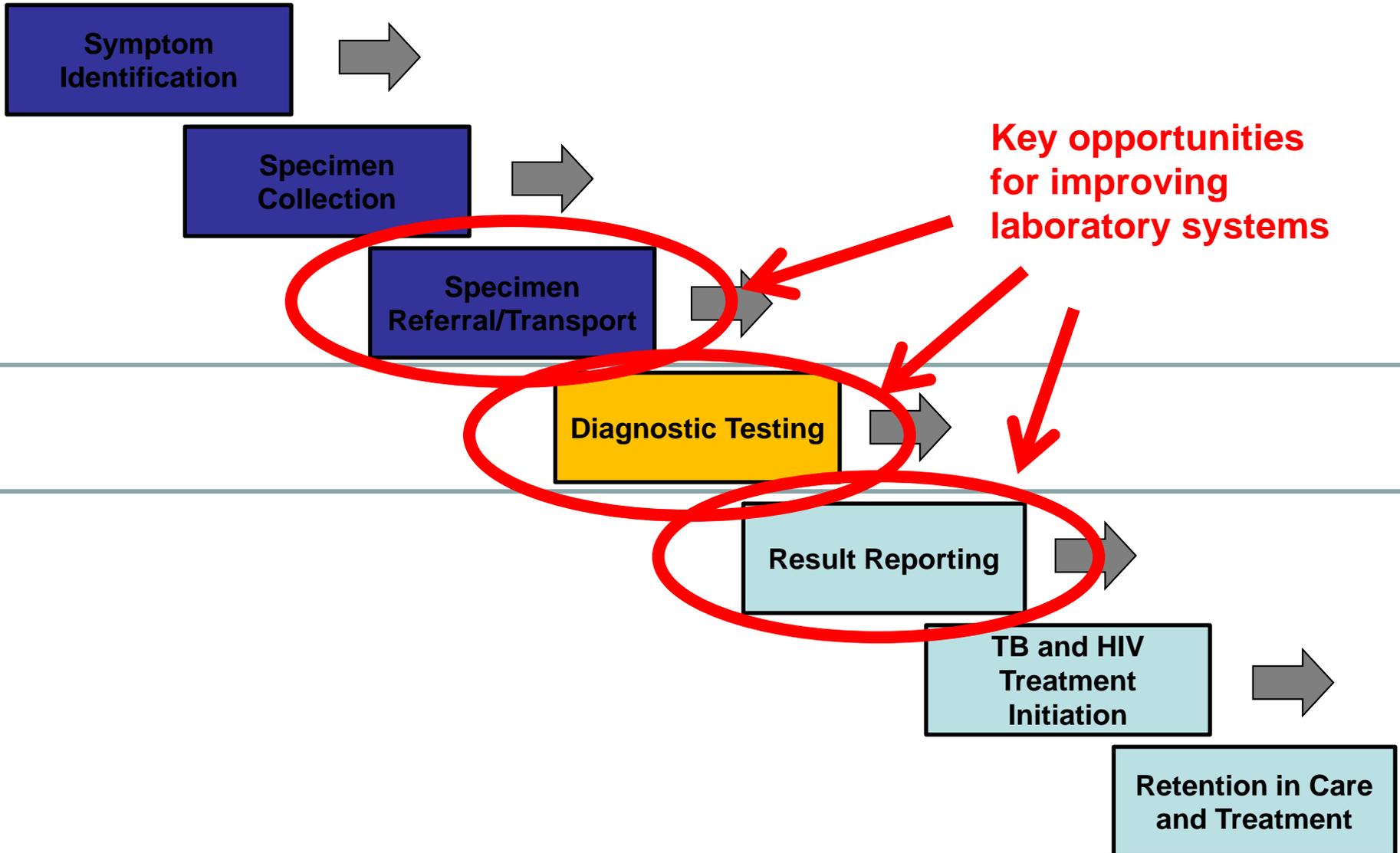


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TB and HIV Integrated Systems Strengthening

Acknowledgement: Heather Alexander, CDC Atlanta

Sensitive and Rapid Tests are Necessary...but not Sufficient





PEPFAR

Integrated Laboratory Systems Across Disease Areas

